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| APPLICATION NO. | FILING DATE | FIRST NAMED INVENTOR | ATTORNEY DOCKET NO. | CONFIRMATION NO. |
|---|-------------|----------------------|---------------------|------------------|
| 09/030,571 | 02/24/1998 | CHARLES R. CANTOR | 25491-2401G | 7542 |
| 20985 | 7590 | 11/03/2004 | EXAMINER | |
| FISH & RICHARDSON, PC 12390 EL CAMINO REAL SAN DIEGO, CA 92130-2081 | | | FORMAN, BETTY J | |
| | | ART UNIT | PAPER NUMBER | |
| | | 1634 | | |

DATE MAILED: 11/03/2004

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary

| | | |
|--|-------------------------------|-------------------------------|
| | Application No. 09/030,571 | Applicant(s) CANTOR ET AL. |
| | Examiner BJ Forman | Art Unit 1634 |

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --
Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1) Responsive to communication(s) filed on 17 August 2004.

2a) This action is **FINAL**. 2b) This action is non-final.

3) Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4) Claim(s) 70,72-79,92-94,123,124,127-133 and 135-138 is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5) Claim(s) _____ is/are allowed.

6) Claim(s) 70 72-79 92-94 123-124 127-133 135-138 is/are rejected.

7) Claim(s) _____ is/are objected to.

8) Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9) The specification is objected to by the Examiner.

10) The drawing(s) filed on _____ is/are: a) accepted or b) objected to by the Examiner.
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11) The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12) Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
a) All b) Some * c) None of:
1. Certified copies of the priority documents have been received.
2. Certified copies of the priority documents have been received in Application No. _____.
3. Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) Notice of References Cited (PTO-892)
2) Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08)
Paper No(s)/Mail Date _____.

4) Interview Summary (PTO-413)
Paper No(s)/Mail Date. _____.
5) Notice of Informal Patent Application (PTO-152)
6) Other: _____.

DETAILED ACTION

Continued Examination Under 37 CFR 1.114

1. A request for continued examination under 37 CFR 1.114, including the fee set forth in 37 CFR 1.17(e), was filed in this application after final rejection. Since this application is eligible for continued examination under 37 CFR 1.114, and the fee set forth in 37 CFR 1.17(e) has been timely paid, the finality of the previous Office action has been withdrawn pursuant to 37 CFR 1.114. Applicant's submission filed on 17 August 2004 has been entered.

Status of the Claims

2. This action is in response to papers filed 17 August 2004 in which the specification and claims 70, 73-75, 124, 127, 136, 137 were amended. The amendments have been thoroughly reviewed and entered.

The previous rejections in the Office Action dated 18 February 2004, not reiterated below, are withdrawn in view of the amendments. Applicant's arguments have been thoroughly reviewed and are discussed below as they apply to the instant grounds for rejection. New grounds for rejection are discussed.

Claims 70, 72-79, 92-94, 123-124, 127-133, 135-138 are under prosecution.

Claim Rejections - 35 USC § 112

35 U.S.C. 112: First paragraph

3. The following is a quotation of the first paragraph of 35 U.S.C. 112:

The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

4. Claims 70, 72-73 and 77-79 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

a. The recitation "wherein the variable sequence is not at the 5' terminus or 3' terminus" is added to the newly amended independent claim 70 (from which Claims 72, 73, 77-79 depend). However, the specification fails to define or provide any disclosure to support such claim recitation.

Applicant points to page 20, line 25 through page 21, line 8 for support for the newly added limitation. However, page 21, line 2 of the cited passage specifically teaches "a random sequence of length R at the 5'-terminus." As such, the cited passage contradicts Applicant's asserted support because the passage teaches the random sequence IS at the 5'-terminus. In further arguments (pages 13-15), Applicant points to page 6 lines 3-6 and 16-24. However, as discussed in the previous Office Action, the passage merely teaches: "a random nucleotide sequence within the single-stranded portion" and a "random internal sequence". Nowhere in the cited passages does the specification teach a random sequence not at the 5' or 3' terminus as instantly claimed. The cited passages define the random sequences as being within and/or internal to the single stranded portion. The random sequence, as defined in the specification, encompasses a random sequence anywhere within the single-stranded portion encompassing the termini, not excluding it as asserted. Nowhere in the cited passages, or specification as a whole, is the random sequence defined as excluding the termini as claimed. Hence, the amendments discussed above constitute new matter.

To illustrate the negative limitation, Applicant points to Table 5 on page 48 wherein random sequences (as underlined) are exemplified as not at the termini. The argument is acknowledged but is not found persuasive. First, the sequences presented on page 14 of Applicant's response incorrectly illustrates the sequences in Table 5 of the specification. The specification illustrates ONE underlined nucleotide, not two as presented on page 14 of the response and certainly not a sequence as claimed. Furthermore, the sequences in Table 5 of the specification and page 14 of the response do not illustrate a random sequence. In contrast the underlined nucleotides are mismatch-specific, not random as claimed. As such, the sequences of Table 5 are known sequences complementary to known mismatches and therefore the direct opposite of random sequences as claimed. Nowhere in the cited passages or specification is the random sequence defined as not at the 5' or 3' termini.

Any negative limitation or exclusionary proviso must have basis in the original disclosure. If alternative elements are positively recited in the specification, they may be explicitly excluded in the claims. See *In re Johnson*, 558 F.2d 1008, 1019, 194 USPQ 187, 196 (CCPA 1977) ("[the] specification, having described the whole, necessarily described the part remaining."). See also *Ex parte Grasselli*, 231 USPQ 393 (Bd. App. 1983), aff'd mem., 738 F.2d 453 (Fed. Cir. 1984). The mere absence of a positive recitation is not basis for an exclusion. Any claim containing a negative limitation which does not have basis in the original disclosure should be rejected under 35 U.S.C. 112, first paragraph as failing to comply with the written description requirement (see MPEP 2173.05(i)).

35 U.S.C. 112: Second paragraph

5. The following is a quotation of the second paragraph of 35 U.S.C. 112:

The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

6. Claims 73, 76, 127-133, 135, 137 and 138 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claim 73 is indefinite for the recitation “the solid support” because the recitation lacks proper antecedent basis in Claim 70. It is suggested that the claim be amended to provide proper antecedent basis.

Claim 76 is indefinite for the recitation “the solid support” because the recitation lacks proper antecedent basis in Claim 74. It is suggested that the claim be amended to provide proper antecedent basis.

Claims 132 and 133 are each indefinite for the recitation “the solid support” because the recitation lacks proper antecedent basis in Claim 127. It is suggested that the claims be amended to provide proper antecedent basis.

Claims 127-133, 135, 137 and 138 are indefinite in Claim 127 for the recitation “the four nucleic acid bases” because the recitation lacks proper antecedent basis in the claim. Therefore it is unclear which four (of the at least five) bases are being described.

Claim Rejections - 35 USC § 102

7. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless –

(e) the invention was described in (1) an application for patent, published under section 122(b), by another filed in the United States before the invention by the applicant for patent or (2) a patent granted on an application for patent by another filed in the United States before the invention by the applicant for patent, except that an international application filed under the treaty defined in section 351(a) shall have the effects for purposes of this subsection of an application filed in the United States only if the international application designated the United States and was published under Article 21(2) of such treaty in the English language.

8. Claims 70, 72, 74, 76-79, 92-94, 124 and 136 are rejected under 35 U.S.C. 102(e) as being anticipated by Deugau et al (U.S. Patent No. 5,508,169, filed 6 April 1990).

Regarding Claim 70, Deugau et al disclose an array of nucleic acid probes (i.e. complete panel of indexing linkers) wherein each probe has a double-stranded portion and a terminal single stranded portion comprising a variable nucleotide sequence within the single-stranded portion (Column 11, lines 14-25, Fig. 2 and Claim 33). Furthermore, Deugau et al the Type IIS enzymes used to produce the single-stranded regions produce “any of the possible permutations and combinations of nucleotides” (Column 10, lines 14-18). Hence, the single stranded regions are not produced with any order, but are instead, random. Furthermore, the random portions are within the single-stranded regions as defined in the instant specification.

Additionally, because the single stranded portion of Deugau et al have a terminal nucleotide and the number of nucleotides between the terminal nucleotide and the double stranded portion of the probe varies, the variable single stranded sequence would be interpreted as being not at the terminus, but instead between the terminus and the double stranded portion.

The courts have stated that claims must be given their broadest reasonable interpretation consistent with the specification *In re Morris*, 127 F.3d 1048, 1054-55, 44 USPQ2d 1023, 1027-28 (Fed. Cir. 1997); *In re Prater*, 415 F.2d 1393, 1404-05, 162 USPQ 541, 550-551 (CCPA 1969); and *In re Zletz*, 893 F.2d 319, 321-22, 13 USPQ2d 1320, 1322 (Fed. Cir. 1989) (see MPEP 2111). Given the broadest reasonable interpretation in view of the claim language and specification, Deugau et al teach the probes as claimed.

Regarding Claim 72, Deugau et al disclose the array wherein the double-stranded portion (i.e. common sequence # 1026, # 1504 and # 1701) is between about 3-20 nucleotide

and the single stranded portion is between about 3-20 nucleotides (Columns 15-16, Table I and Table II).

Regarding Claim 74, Deugau et al teach an array of probes comprising a first nucleic acid hybridized to the second nucleic acid forming a hybrid having a double-stranded portion and a single-stranded portion (Column 11, lines 14-25; Columns 15-16, Table I and Table II; Fig. 2; and Claim 33).

Furthermore, Deugau et al the Type IIS enzymes used to produce the single-stranded regions produce “any of the possible permutations and combinations of nucleotides” (Column 10, lines 14-18). Hence, the single stranded regions are not produced with any order, but are instead, random.

The courts have stated that patentability of a product is based on the product, not method of making the product. Because Deugau et al teach the product i.e. array of probes, the disclose the instantly claimed array.

“[E]ven though product-by-process claims are limited by and defined by the process, determination of patentability is **based on the product itself**. The patentability of a product does not depend on its method of production. If the product in the product-by-process claim is the same as or obvious from a product of the prior art, the claim is unpatentable even though the prior product was made by a different process.” In re Thorpe, 777 F.2d 695, 698, 227 USPQ 964, 966 (Fed. Cir. 1985) see MPEP 2113.

Regarding Claim 76, Deugau et al teach the array wherein the solid support is a two-dimensional matrix with multiple probe binding sites i.e. the probes are attached to spatially segregated solid phase substrates (Column 10, lines 45-51).

Regarding Claim 77, Deugau et al teach the array wherein the probes are labeled with a detectable label (Claim 27).

Regarding Claim 78, Deugau et al teach the array wherein the label comprises a radioisotope or fluorescent chemical (Claims 27 & 28).

Regarding Claim 79, Deugau et al teach the array wherein the nucleic acids are DNA (Claims 25 and 33).

Regarding Claim 92, Deugau et al teach the array wherein the probes are labeled with a detectable label (Claim 27).

Regarding Claim 93, Deugau et al teach the array wherein the label comprises a radioisotope or fluorescent chemical (Claims 27 & 28).

Regarding Claim 94, Deugau et al teach the array wherein the nucleic acids are DNA (Claims 25 and 33).

Regarding Claim 124, Deugau et al teach the array comprising about 4^r different nucleic acid probes (i.e. complete panel of indexing linkers) (Column 11, lines 14-25).

Regarding Claim 136, Deugau et al teach the array wherein the constant portion includes an enzyme restriction site (Column 6, lines 1-21).

Response to Arguments

9. Applicant argues that Deugau et al do not teach a probe having a random sequence not at the terminus. The argument has been considered. However, as stated above, the specification defines the instant probes as having the random sequence within the single-stranded region. Therefore, Deugau et al teach the probes as defined in the specification.

Applicant argues that Deugau et al does not teach the probes as defined in Claim 74 wherein an oligonucleotide is ligated to the random sequence providing a single-stranded region of 7 to 30 nucleotides. The argument has been considered but is not found persuasive because the argument is not commensurate in scope with the claims. In contrast to Applicant's assertion, the claims do not require a single-stranded region of 7 to 30 nucleotides. The claims are drawn to a first sequence of 15-25 hybridized to a second, longer sequence of 20-30 wherein the longer sequence is ligated to a oligo of 4 to 20 nucleotides. There are many examples whereby the probe does not have a single-stranded region of 7 to 30 nucleotides as asserted. For example, if the first sequence is 25, the second sequence is 26

and the oligo is 4, the single stranded region is 5. Deugau teaches a single-stranded region of 5 nucleotides (Column 9, lines 28-33). This is but one of the many combinations encompassed by the teaching of Deugau.

Claim Rejections - 35 USC § 103

10. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

11. Claim 73, 123 are rejected under 35 U.S.C. 103(a) as being unpatentable over Deugau et al (U.S. Patent No. 5,508,169, filed 6 April 1990) in view of Brenner et al (Proc. Natl. Acad. Sci. USA, 1989, 86: 88902-8906).

Regarding Claims 73, 123, Deugau et al disclose the array of nucleic acid probes (i.e. complete panel of indexing linkers) wherein each probe has a double-stranded portion at the 3' terminus, a single stranded portion at the 5' terminus and a random nucleotide sequence of length R within the single-stranded portion (Column 11, lines 14-25, Fig. 2 and Claim 33) wherein the probes are immobilized to a solid support (Column 11, lines 14-25) but they do not specifically teach the means by which the probes are immobilized. However, coupling agents e.g. biotin/streptavidin immobilization was well known in the art at the time the claimed invention was made as taught by Brenner et al who teach that biotin/streptavidin provides a versatile means of capture immobilization (page 8904, second full paragraph). It would have been obvious to one of ordinary skill in the art at the time the claimed invention was made to apply the biotin/streptavidin of Brenner et al to the immobilization of Deugau et al based on

et al and to immobilize the probes onto plastic or resin support based on the suggestion of Deugau et al (Column 10, lines 45-51 and Claim 26) thereby utilizing well known supports for the expected benefits of successful immobilization.

Response to Arguments

14. Applicant states that Deugau et al does not teach an array of probes comprising a random sequence not at the terminus. The argument has been considered but is not found persuasive. As stated above, Deugau et al teach the single-stranded portion is random. Hence, Ghosh is not relied upon for this element. Applicant further argues that Ghosh does not cure the deficiencies of Deugau because they do not teach a random sequence not at the termini. The argument has been considered but is not found persuasive for the reasons stated above.

Conclusion

15. Claims 127-133, 135, 137, 138 are free of the prior art of record and may be placed in condition for allowance following resolution of the above rejections.

16. No claim is allowed.

17. Any inquiry concerning this communication or earlier communications from the examiner should be directed to BJ Forman whose telephone number is (571) 272-0741. The examiner can normally be reached on 6:00 TO 3:30.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Gary Jones can be reached on (571) 272-0745. The fax phone number for the organization where this application or proceeding is assigned is 703-872-9306.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you

the teaching of Brenner et al to thereby provide versatile capture immobilization (page 8904, second full paragraph).

Response to Arguments

12. Applicant states that Deugau et al does not teach an array of probes comprising a random sequence not at the terminus. The argument has been considered but is not found persuasive. As stated above, Deugau et al teach the single-stranded portion is random. Hence, Brenner is not relied upon for this element. Applicant further argues that Brenner does not cure the deficiencies of Deugau because they do not teach a random sequence not at the termini. The argument has been considered but is not found persuasive for the reasons stated above.

13. Claim 75 is rejected under 35 U.S.C. 103(a) as being unpatentable over Deugau et al (U.S. Patent No. 5,508,169, filed 6 April 1990) in view of Ghosh et al (Nucleic Acids Research, 1987, 15: 5353-5372).

Regarding Claim 75, Deugau et al teach an array of probes comprising a first nucleic acid hybridized to the second nucleic acid forming a hybrid having a double-stranded portion and a single-stranded portion (Column 11, lines 14-25; Columns 15-16, Table I and Table II; Fig. 2; and Claim 33). wherein the probes are fixed to a solid support as taught by Ghosh et al (Column 10, lines 45-51 and Claim 26) but they do not specifically teach the material from which the solid support is made. However, Ghosh et al teach their solid support is selected from plastics and resins (page 5356, first full paragraph-page 5357, last paragraph).

It would have been obvious to one of ordinary skill in the art at the time the claimed invention was made to apply the solid supports of Ghosh et al to the immobilization of Deugau

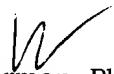
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have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to (571) 272-0547.

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For all other customer support, please call the USPTO Call Center (UCC) at 800-786-9199.


BJ Forman, Ph.D.
Primary Examiner
Art Unit: 1634
October 26, 2004